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Nicholas J. Seay
Quarles & Brady LLP
P.O. Box 2113
Madison, WI 53701-2113

EXAMINER	
SULLIVAN, DANIEL M	

ART UNIT	PAPER NUMBER
1636	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/627,245	THOMSON ET AL.	
	Examiner	Art Unit	
	Daniel M. Sullivan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-15 is/are pending in the application.

4a) Of the above claim(s) 4-6 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-3,7-15 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 25 July 2003 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This is the First Office Action on the Merits of the application filed 25 July 2005, which claims benefit of provisional application 60/399,330 filed 26 July 2002. The preliminary amendment filed 13 January 2004 has been entered. Claims 1-15, as originally filed, are pending.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-3 and 7-15, drawn to a method for testing agents for effect on human cardiac cells comprising measuring the transmembrane action potential, classified in class 435, subclass 29.

II. Claims 4-6, drawn to a method for testing agents for their effect on human cardiac cells comprising forming embryoid bodies and measuring contraction of the embryoid body, classified in class 435, subclass 29.

The inventions are distinct, each from the other because of the following reasons:

The processes of Groups I and II are distinct because they are not disclosed as capable of use together in a single process and each method is limited to comprising distinct process steps to which the other method is not limited. The process of Group I is limited to measuring the transmembrane action potential and does not comprise measuring contraction of an embryoid body. Conversely, the process of Group II is limited to measuring the contraction of an embryoid body and does not comprise measuring transmembrane action potential. Therefore, each process comprises a distinct mode of operation, function and effect relative to the process of the other Group.

As each method is limited to comprising elements to which the other method is not limited, examination of each method requires a separate search for those elements that distinguish the respective methods. In addition, because each method encompasses subject matter not encompassed by the other method, a determination that any one method is patentable over the art does not adequately support patentability of the other method. Therefore, patentability of each method must be determined separately and examining the methods together in a single application imposes a serious burden on the Office.

During a telephone conversation with Nicholas Seay on 28 July 2005 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-3 and 7-15. Affirmation of this election must be made by applicant in replying to this Office action. Claims 4-6 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Specification

The disclosure is objected to because of the following informalities: Paragraph 44 of the specification contains reference to Figures but does not specify which figures are being referred to (see especially lines 5 and 9). Likewise, the paragraph makes reference to a Table; however, the disclosure does not appear to contain a Table.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2, 8, 11 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are indefinite in the recitation of "atrial-type, ventricular-type and nodal-type". The most relevant teaching in the specification appears in paragraph 00044 and reads as follows:

> [00044] To characterize the types of cardiomyocytes in the EBs, we examined the shape and properties of action potentials from 105 stable impalements of 20 different EBs. At the time window of differentiation that we studied (40-95 days), there was clear heterogeneity in the morphology of the action potentials; however, the action potentials could be classified into 3 major types: nodal-like, embryonic atrial-like, and embryonic ventricular-like (Fig.). This classification was based on the properties of the action potential as measured by the maximum rate of rise of the action potential (dv/dtmax), the action potential duration (APD), action potential amplitude (APA), and prominence of phase 4 depolarization as summarized in the Table. Nodal-like action potentials (Fig.) were characterized by prominent phase-4 depolarization, slow upstroke (dv/dtmax), and a smaller APA. Embryonic ventricular-like action potentials could be distinguished by the presence of a significant plateau phase of the action potential resulting in a significantly longer duration compared to the more triangular shaped embryonic-atrial action potentials. In addition, embryonic ventricular-like action potentials generally showed a trend for slower spontaneous rates of activity the longer the EBs were maintained in culture from 40 to 95 days.

The description provided is vague and relies on relative properties such as "prominent phase-4 depolarization, slow upstroke and smaller APA". Although the paragraph makes reference to a Table, there is no Table in the application. As there are no concrete definitions of terms such as "prominent", "slow" and "smaller" and no specific values provided for dv/dtmax, APD, APA or prominence of phase 4 depolarization which define a cardiomyocyte as atrial-type, ventricular-type or nodal-type, the skilled artisan would not know whether a cell having a given

dv/dtmax, APD, APA or prominence of phase 4 depolarization would meet the limitations of an "atrial-type", "ventricular-type" or "nodal-type" cardiomyocyte. Therefore, the metes and bounds of the claimed subject matter are unclear.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 2, 7, 8, 10, 11, 13 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by either one of Bosch *et al.* (1998) *Cardiovasc. Res.* 38:441-450 or Li *et al.* (1996) *Circ. Res.* 78:689-696 (citations of specific teachings from Li *et al.* refer to the online publication mailed with this action).

Independent claim 1 is directed to a method comprising culturing cardiomyocytes derived from human embryonic stem cells, measuring the transmembrane action potential of at least one cardiomyocyte, exposing the cardiomyocyte to a test agent and observing whether the action potential of the cardiomyocyte changes after exposure to the agent.

Independent claim 7 is comprises the steps recited in claim 1 and further comprises inserting an electrode into at least one cardiomyocyte in culture. The claim further recites that the action potential is observed for a change in duration triggered by the agent.

Independent claim 10 comprises the steps of claim 1 and further comprises obtaining a chart of the transmembrane action potential over time. The claim further recites that the action potential is observed for a delayed after polarization event triggered by the agent.

Independent claim 13 comprises the steps of claim 1 and further comprises obtaining a chart of the transmembrane action potential of a plurality of the cardiomyocyte over time. The claim further recites that the system is observed for a long QT syndrome triggered by the agent.

As all human cardiomyocytes are "derived from human embryonic stem cells" (*i.e.*, all human hearts are derived from embryos), the cardiomyocytes of the claims are construed as reading on any human cardiomyocyte.

Bosch *et al.* teaches a method comprising measuring the transmembrane action potential of human cardiomyocytes in culture (see especially section 3.4 on page 447 and Figure 8 and the caption thereto). Bosch *et al.* further teaches exposing the cardiomyocytes to an agent and observing whether the action potential of the cardiomyocyte changes after exposure (see especially Figure 8). In view of the broad construction of "cardiomyocytes derived from human embryonic stem cells", the method of Bosch *et al.* comprises each of the limitations of the instant claim 1.

As the action potentials were measured using a whole cell voltage-clamp technique, the method of Bosch *et al.* comprises inserting an electrode into a cardiomyocyte (see especially

section 2.2 on page 443) and observing whether the action potential duration is changed by the agent (see especially Figure 8B) as recited in independent claim 7.

In Figure 8A, Bosch *et al.* teaches a chart of the transmembrane action potential over time according to claims 10 and 13. Furthermore, in the caption to Figure 8B, Bosch *et al.* shows averaged data indicating that the measurements were obtained from a plurality of cardiomyocytes according to claim 13. Although Bosch *et al.* does not explicitly teach that the cardiomyocytes were observed for delayed after polarization or long QT syndrome, the observing step of Bosch *et al.* is the same as observing for delayed after polarization or long QT syndrome. In other words, delayed after polarization or long QT syndrome would be observed in the method of Bosch *et al.* if those phenomena were present. Therefore, the method of Bosch *et al.* is the same as the method of independent claims 10 and 13.

Claims 2, 8, 11 and 14 limit the cardiomyocyte of claims 1, 7, 10 and 13 to a ventricular-type. Although the metes and bounds of the limitation are unclear, the ventricular myocytes of Bosch *et al.* (see especially the caption to Figure 8), are presumed to be encompassed by the ventricular cardiomyocytes of the instant claims. Therefore, the claims are anticipated by Bosch *et al.*

Li *et al.* teaches a method comprising measuring the transmembrane action potential of human cardiomyocytes in culture (see especially the paragraph bridging pages 3-4, the second full paragraph on page 5, figure 1 and the caption thereto). Li *et al.* further teaches exposing the cardiomyocytes to an agent and observing whether the action potential of the cardiomyocyte changes after exposure (see especially Figure 1). In view of the broad construction of

"cardiomyocytes derived from human embryonic stem cells", the method of Li *et al.* comprises each of the limitations of the instant claim 1.

As the action potentials were measured using a whole cell voltage-clamp technique, the method of Li *et al.* comprises inserting an electrode into a cardiomyocyte (see especially section entitled "Data Acquisition and Analysis") and observing whether the action potential duration is changed by the agent (see especially Figure 1D) as recited in independent claim 7.

In Figure 1D, Li *et al.* teaches a chart of the transmembrane action potential over time according to claims 10 and 13. Furthermore, in the second full paragraph on page 5, Li *et al.* teaches that the results shown in Figure 1D are typical, indicating that the measurements were obtained from a plurality of cardiomyocytes according to claim 13. Although Li *et al.* does not explicitly teach that the cardiomyocytes were observed for delayed after polarization or long QT syndrome, as discussed above, the observing step of Li *et al.* is the same as observing for delayed after polarization or long QT syndrome. Therefore, the method of Li *et al.* is the same as the method of independent claims 10 and 13.

Finally, the ventricular myocytes of Li *et al.* (see especially the paragraph bridging 3-4), are presumed to be encompassed by the ventricular cardiomyocytes of the instant claims. Therefore, the claims are anticipated by Li *et al.*

Claims 1, 2, 10, 11, 13 and 14 are rejected under 35 U.S.C. 102(e) as being anticipated by Gepstein *et al.* Pub. No. 2005/0037489 (effective filing date 20 July 2001; evidenced by US provisional application 60/306,462).

Gepstein *et al.* teaches a method of culturing cardiomyocytes derived from human embryonic stem cells comprising permitting human embryonic stem cells to form embryoid bodies (see especially the section entitled "ES cell preparation and production of EBs" beginning on page 3 of the '462 provisional application).

In the first paragraph on page 6 of the '462 application, Gepstein *et al.* teaches a method for measuring transmembrane action potentials in cardiomyocytes derived from the ES cells comprising plating the embryoid bodies comprising human cardiomyocytes on multielectrode arrays and in the first full paragraph on page 10, Gepstein *et al.* teaches a method wherein cardiomyocytes are exposed to various agents and the action potential of the cardiomyocytes are observed for changes. Furthermore, in the paragraph bridging pages 36-37 of the '462 application, Gepstein *et al.* teaches that the cardiomyocytes produced by the method "can be used as a testing system for evaluating the toxicity, teratogenicity and efficacy of new drugs and chemicals and thus may serve as an attractive screening tool with wide spread applications in the pharmaceutical industry" and "[u]sing this system it is possible to study the short and long-term effects of drugs on pacemaker activity".

Thus, Gepstein *et al.* teaches a method comprising each of the steps of independent claim 1. Furthermore, Gepstein *et al.* teaches obtaining a chart of the transmembrane action potential according to claims 10 and 13 (see especially Figure1 c. e. and g., and the Figure 1a on the final page (labeled 38(a)). Although Gepstein *et al.* does not explicitly teach that the cardiomyocytes were observed for delayed after polarization or long QT syndrome, the observing step of Gepstein *et al.* is the same as observing for delayed after polarization or long QT syndrome (*Id.*).

Therefore, the method of Gepstein *et al.* is the same as the method of independent claims 10 and 13.

Finally, given the indefinite nature of the limitations "atrial-type", "ventricular-type" and "nodal-type" it is presumed, absent evidence to the contrary, that the myocytes of Gepstein *et al.* are encompassed by the "atrial-type", "ventricular-type" and/or "nodal-type" cardiomyocytes of the instant claims 2, 11 and 14. Therefore, the claims are anticipated by Gepstein *et al.*

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3 and 7-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over any one of Bosch *et al.* (*supra*), Li *et al.* (*supra*) or Carlsson *et al.* (1997) 282:220-227 in view of Gepstein *et al.* (*supra*; as evidenced by US provisional application 60/306,462).

The limitations of claims 1, 2, 7, 8, 10, 11, 13 and 14 and the teachings of Bosch *et al.* (*supra*) and Li *et al.* (*supra*) are described herein above. Bosch *et al.* (*supra*) and Li *et al.* (*supra*) do not teach the method wherein culturing is conduced by permitting the human embryonic stem cells to form embryoid bodies and impaling an embryoid body with an electrode according to the limitations of claims 3, 9, 12 and 15.

Gepstein *et al.* teaches a method of culturing cardiomyocytes derived from human embryonic stem cells comprising permitting human embryonic stem cells to form embryoid bodies (see especially the section entitled "ES cell preparation and production of EBs beginning on page 3 of the '462 provisional application). In the paragraph bridging pages 36-37 of the '462 application, Gepstein *et al.* teaches that the cardiomyocytes produced by the method "can be used as a testing system for evaluating the toxicity, teratogenicity and efficacy of new drugs and chemicals and thus may serve as an attractive screening tool with wide spread applications in the pharmaceutical industry" and "[u]sing this system it is possible to study the short and long-term effects of drugs on pacemaker activity".

Thus, the teachings of Gepstein *et al.* demonstrate that a method of culturing cardiomyocytes comprising permitting human ES cells to form embryoid bodies was known in

the art at the time the invention was made, and that these cells would be useful to evaluate the toxicity of new drugs and drug effects on pacemaker activity.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the cardiomyocytes cultured according to the teachings of Gepstein *et al.* for the cardiomyocytes used in the methods of Bosch *et al.* or Li *et al.* according to the limitations of the instant claims.

Motivation to combine the teachings of Bosch *et al.* or Li *et al* with the teachings of Gepstein *et al.* can be found in Gepstein *et al.*, who teaches, "[t]he major advantage of this model is that it is the only existing long-term in vitro model for human tissue that is currently available". Thus, one would be motivated to use the cardiomyocyte culture system of Gepstein *et al.* to obtain the expected benefit of a long term *in vitro* model, which would obviate the relatively difficult procedure of obtaining cardiomyocytes from human patients as taught in the methods of Bosch *et al.* and Li *et al.*

Absent evidence to the contrary, one would have a reasonable expectation of success in combining these teachings in view of the demonstration by Gepstein *et al.* that the cardiomyocytes obtained according to the method described therein exhibit cardiomyocyte action potentials (see especially Figure1 and the Figures on the final page (labeled 38(a)).

With regard to the limitation, "measuring includes impaling an embryoid body with an electrode" of claims 3, 9, 12 and 15, this limitation would be obvious in view of the fact that the methods of measuring transmembrane action potential of Bosch *et al.* or Li *et al.* comprise contacting a single cell with an electrode. As the cardiomyocytes cultured according to the

method of Gepstein *et al.* are comprised in an embryoid body, contacting the cell with an electrode would comprise impaling the embryoid body comprising the cells.

For these reasons, the invention of the instant claims, as a whole, would have been obvious to one of ordinary skill in the art at the time the invention was made. Therefore, the claims are properly rejected under 35 USC §103(a) as obvious over the art.

Claims 1-3 and 7-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carlsson *et al.* (1997) *J. Pharmacol. Exp. Ther.* 282 :220-227 in view of Gepstein *et al.* (*supra*; as evidenced by US provisional application 60/306,462).

The limitations of the claims are described herein above.

Carlsson *et al.* teaches a method comprising measuring the transmembrane action potential of cardiomyocytes in culture (see especially the paragraph bridging pages 282-283, Figures 8 and 9 and the captions thereto). Carlsson *et al.* further teaches exposing the cardiomyocytes to an agent and observing whether the action potential of the cardiomyocyte changes after exposure (see especially Figures 8 and 9). Thus, Carlsson *et al.* teaches a method comprising all of the limitations of the instant claim 1 except for cardiomyocytes that are derived from human ES cells.

As the action potentials were measured using a whole cell voltage-clamp technique, the method of Carlsson *et al.* comprises inserting an electrode into a cardiomyocyte (see especially the third and fourth paragraphs on page 282) and observing whether the action potential duration is changed by the agent (see especially Figure 9) as recited in independent claim 7. Thus,

Carlsson *et al.* teaches a method comprising all of the limitations of the instant claim 7 except for cardiomyocytes that are derived from human ES cells.

In Figures 8 and 9, Carlsson *et al.* teaches a chart of the transmembrane action potential over time according to claims 10 and 13. Furthermore, in the paragraph bridging pages 224-225, Carlsson *et al.* shows averaged data indicating that the measurements were obtained from a plurality of cardiomyocytes according to claim 13. Still further, in Figure 9, Carlsson *et al.* teaches observing the action potentials for delayed after polarization events triggered by cisapride according to claim 10. Although Carlsson *et al.* does not explicitly teach that the cardiomyocytes were observed for long QT syndrome, the observing step of Carlsson *et al.* is the same as observing for long QT syndrome (*Id.*). Thus, Carlsson *et al.* teaches a method comprising all of the limitations of the instant claims 10 and 13 except for cardiomyocytes that are derived from human ES cells.

Gepstein *et al.* teaches a method of culturing cardiomyocytes derived from human embryonic stem cells comprising permitting human embryonic stem cells to form embryoid bodies (see especially the section entitled "ES cell preparation and production of EBs beginning on page 3 of the '462 provisional application). In the paragraph bridging pages 36-37 of the '462 application, Gepstein *et al.* teaches that the cardiomyocytes produced by the method "can be used as a testing system for evaluating the toxicity, teratogenicity and efficacy of new drugs and chemicals and thus may serve as an attractive screening tool with wide spread applications in the pharmaceutical industry" and "[u]sing this system it is possible to study the short and long-term effects of drugs on pacemaker activity".

Thus, the teachings of Gepstein *et al.* demonstrate that a method of culturing cardiomyocytes comprising permitting human ES cells to form embryoid bodies was known in the art at the time the invention was made, and that these cells would be useful to evaluate the toxicity of new drugs and drug effects on pacemaker activity.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the cardiomyocytes cultured according to the teachings of Gepstein *et al.* for the cardiomyocytes used in the method of Carlsson *et al.* according to the limitations of the instant claims.

Motivation to combine the teachings of Carlsson *et al.* can be found in the nature of the problem to be solved by the method of Carlsson *et al.*, which is to characterize potential cardiotoxic properties of medications to be used in treating humans (see especially the introductory discussion on pages 220-221) and from Gepstein *et al.*, who teaches, "[t]he major advantage of this model is that it is the only existing long-term in vitro model for human tissue that is currently available". Thus, one would be motivated to use the cardiomyocyte culture system of Gepstein *et al.* to obtain the expected benefit of a long term human *in vitro* model, which would provide human cardiomyocytes for characterization of drugs to be used in humans and which would obviate the relatively difficult procedure of obtaining cardiomyocytes from rabbits taught in the methods of Bosch *et al.* and Li *et al.*

Absent evidence to the contrary, one would have a reasonable expectation of success in combining these teachings in view of the demonstration by Gepstein *et al.* that the cardiomyocytes obtained according to the method described therein exhibit cardiomyocyte action potentials (see especially Figure1 and the Figures on the final page (labeled 38(a)).

With regard to the limitations of claims 2, 8, 11 and 14, given the indefinite nature of the limitations "atrial-type", "ventricular-type" and "nodal-type" it is presumed, absent evidence to the contrary, that the myocytes of Gepstein *et al.* are encompassed by the "atrial-type", "ventricular-type" and/or "nodal-type" cardiomyocytes of the instant claims 2, 11 and 14. Therefore, the claims are anticipated by Gepstein *et al.*

With regard to the limitation, "measuring includes impaling an embryoid body with an electrode" of claims 3, 9, 12 and 15, this limitation would be obvious in view of the fact that the methods of measuring transmembrane action potential of Carlsson *et al.* comprises contacting a single cell with an electrode. As the cardiomyocytes cultured according to the method of Gepstein *et al.* are comprised in an embryoid body, contacting the cell with an electrode would comprise impaling the embryoid body comprising the cells.

For these reasons, the invention of the instant claims, as a whole, would have been obvious to one of ordinary skill in the art at the time the invention was made. Therefore, the claims are properly rejected under 35 USC §103(a) as obvious over the art.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 571-272-0779. The examiner can normally be reached on Monday through Friday 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Daniel M. Sullivan, Ph.D.
Examiner
Art Unit 1636

DANIEL M. SULLIVAN
PATENT EXAMINER